PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference M/43348-PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/14422	International filing date *(day/month/year)* 17.12.2003	Priority date *(day/month/year)* 18.12.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/4178		
Applicant FERRER INTERNACIONAL, S.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
01.07.2004	17.03.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Beeck, M Telephone No. +49 89 2399-8473

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/14422

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-14 as originally filed

Claims, Numbers

1-27 received on 28.02.2005 with letter of 28.02.2005

Drawings, Sheets

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 26,27

   because:

   ☒ the said international application, or the said claims Nos. 26,27 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-27
	No:	Claims	
Inventive step (IS)	Yes:	Claims	5-17
	No:	Claims	1-4,18-27
Industrial applicability (IA)	Yes:	Claims	1-25
	No:	Claims	

2. Citations and explanations

see separate sheet

D1: WO 03/032948 A (MCNEIL-PPC, INC.) 24 April 2003 (2003-04-24)

D2: J. TORRES ET AL: "Sertaconazole in the treatment of mycoses; from dermatology to gynaecology" INTERNATIONAL JOURNAL OF GYNAECOLOGY AND OBSTETRICS, vol. 71, no. S1, December 2000 (2000-12), pages S3-S20, XP002250812 New York (US)

SECTION III:

Claims 26 and 27 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

SECTION V:

1) The examination has been carried out assuming that the priority is valid, so that P-document D1 has not been taken into consideration.

2) The subject-matter of the claims is novel.

3) Closest prior art document for the assessment of inventive step is document D2 which already describes the use of 2% sertaconazole for the treatment of vulvovaginal candidiasis (see the abstract and chapters 2 to 5).

The subject-matter of the claims differs therefrom in that the proportion of sertaconazole is higher than 2% and does not exceed 10%.

Hence, the problem to be solved was to provide a composition for the treatment of vaginal candidiasis, using a higher concentration of the active ingredient.

However, the routine experimentation to optimize the required amounts of ingredients of known compositions for a known use falls within the normal capacity of the average skilled person so that prima facie the subject-matter of the claims does not involve an inventive step.

But the figure in conjunction with examples 1 and 2 in the present patent shows the advantageous property of a composition containing 6% sertaconazole.

Therefore the subject-matter of claim 5 involves an inventive step.

4) However, the presence of an inventive step must be shown over the whole range of the concentration of sertaconazole as claimed, which has not been done.

Therefore the subject-matter of claims 1 to 4 and 18 to 27 does not involve an inventive step (Article 33 (3) PCT).

5) In view of the additional differences from the state of the art the subject-matter of claims 6 to 17 involves an inventive step.

6) For the assessment of the present claims 26 and 27 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

CLAIMS

1. A vaginal mucoadhesive composition for single dose administration, which is a cream or a gel and comprises sertaconazole or one of its pharmaceutically acceptable salts wherein the proportion of sertaconazole or the salt is higher than 2 % and does not exceed 10 %.

2. The composition of claim 1, wherein the proportion of sertaconazole or the salt is from 3 to 10 %.

3. The composition of claim 1 or 2, which is a cream.

4. The composition of any one of claims 1 to 3, wherein the pharmaceutically acceptable salt is sertaconazole nitrate.

5. The composition of claim 4, wherein the proportion of sertaconazole nitrate is from 6 to 7 %.

6. The composition of any one of claims 1 to 5, wherein the cream contains lipophilic excipients, mucoadhesive excipients and one or more preservatives, and the gel dosage form contains mucoadhesive excipients and one or more preservatives.

7. The composition of claim 6, wherein the lipophilic excipients are selected from glyceryl stearates and their derivatives, ketostearyl alcohols, polyoxyethylene glycol ethers of n-alcohols, liquid paraffin, lecithin oil, glycerol and the like.

8. The composition of claim 7, wherein the lipophilic excipients are present in a total proportion of from 10 to 40%.

9. The composition of claim 8, wherein the lipophilic excipients are present in a total proportion of from 30 to 35%.

10. The composition of claim 6, wherein the mucoadhesive excipients are selected from cellulose polymers, gelatin, colloidal anhydrous silica and polyacrylic acid polymers.

11. The composition of claim 10, wherein the mucoadhesive excipients are polyacrylic acid polymers.

12. The composition of claim 11, wherein the polyacrylic acid polymers form a mixture of polyacrylic acid polymer cross-linked with divinyl glycol and acrylic acid polymer cross-linked with sucrose or pentaerythritol allyl esters.

13. The composition of claim 12, wherein the mixture of polyacrylic acid polymer cross-linked with divinyl glycol and acrylic acid polymer cross-linked with sucrose or pentaerythritol allyl esters are present in a proportion of from 0.1 to 3%.

14. The composition of claim 13, wherein the mixture of polyacrylic acid polymer cross-linked with divinyl glycol and acrylic acid polymer cross-linked with

sucrose or pentaerythritol allyl esters are present in a proportion of from 1 to 1.5%.

15. The composition of claim 6, wherein the preservatives are selected from parabens, benzoic acid, sorbic acid, boric acid and the like.

16. The composition of claim 15, wherein the preservatives are present in a total proportion of from 0.01 to 0.3%.

17. The composition of claim 16, wherein the preservatives are present in a total proportion of from 0.1 to 0.2%.

18. The composition of any one of the preceding claims, wherein its content is packed in a single-dose applicator.

19. The composition of claim 18, wherein its capacity is from 4 to 6 ml.

20. The composition of claim 19, wherein its capacity is 5 ml.

21. A kit comprising the composition according to claims 1-20, and a cream composition for vulvar application containing sertaconazole or one of its pharmaceutically acceptable salts.

22. The kit of claim 21, wherein the pharmaceutically acceptable salt is sertaconazole nitrate.

23. The kit of claim 22, wherein sertaconazole nitrate is present in a proportion of from 1 to 3%.

24. The kit of claim 23, wherein sertaconazole nitrate is present in the proportion of 2%.

25. Use of the composition according to claims 1 to 20 for the manufacture of a pharmaceutically acceptable dosage form for the treatment of vulvovaginal candidiasis of the vagina.

26. A method for treating vulvovaginal candidiasis, wherein the composition of claim 1 is administered into the vagina of a subject in need of such treatment in a single dose.

27. The method of claim 26, wherein additionally a composition containing sertaconazole or one of its pharmaceutically acceptable salts is applied to the vulva in single or repeated dose.